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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/527,553	09/09/2005	Paul Dent	ON/4-32678A	9557

1095 7590 05/23/2008

NOVARTIS
CORPORATE INTELLECTUAL PROPERTY
ONE HEALTH PLAZA 104/3
EAST HANOVER, NJ 07936-1080

EXAMINER	
WEBB, WALTER E	

ART UNIT	PAPER NUMBER
1612	

MAIL DATE	DELIVERY MODE
05/23/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/527,553	DENT ET AL.	
	Examiner	Art Unit	
	WALTER E. WEBB	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 February 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3 and 7-9* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3 and 7-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' arguments, filed 2/11/2008, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 103

Claims 1-9 were rejected under 35 USC 103(a) as being un patentable over Grant et al. in view of Carroll et al. and Vrana et al., and in further view of Zimmermann and Pandolfi et al. This rejection is maintained in regard to claims 1, 3 and 7-9. Claims 2 and 4-6 have been cancelled.

Applicant argues that the combinations described in the present application do not yield predictable results and that the outcome of combining two therapeutic agents in unknown in the field of oncology. They discuss in general that combinations have been known to have positive and negative results. However, given that the SAHA and a compound of formula I have been taught in the art to be useful for treating the same disease, leukemia, the artisan would have a reasonable expectation of success in combining the compounds for the treatment of the same disease. The results are

predicatable insofar as the artisan would have a reasonable expectation in successfully treating leukemia.

Applicant argues that the ordinary skilled artisan would not be able to predict the outcome of combining therapeutic agents, such as imatinib and an HDAC inhibitor and that none of the references cited provide the necessary motivation to predict the successful therapeutic benefits of combining imatinib with HDAC inhibitors. First of all, applicant's arguments are not commensurate in scope with the instant claims, as applicant does not claim successful therapeutic benefits of combining imatinib with HDAC inhibitors. Secondly, the references teach that both compounds are useful in treating leukemia and based on *In re Kerkhoven* a prima facie case of obviousness can be made in these instances. Thirdly, Grant provides further motivation to combine these agents by stating the combinations involving imatinib and SAHA "offers significant opportunities for therapeutic advances in the treatment of human malignancies." (See abstract.)

Applicant argues that the data provided in the specification clearly support that the claimed composition is unobvious since they show a synergistic therapeutic effect and synergism is unpredictable to a skilled artisan. However, MPEP § 2143.02 states that obviousness requires only a reasonable expectation of success. The artisan would reasonably expect synergy since both compounds operate via different mechanisms and Grant provides that "[i]t has also become apparent that these novel agents may, in a dose- and sequence-dependent manner, lower the threshold for conventional cytotoxic drug-induced apoptosis, resulting in synergistic interactions."

Applicant's data at pages 5 and 6, supporting increased effect when combining imatinib with SAHA or sodium butyrate is not inconsistent with Grant. Synergism or increased cytotoxic activity is the motivation behind combining imatinib with other compounds such as SAHA. The combination lowers the threshold for conventional cytotoxic drug-induced apoptosis, resulting in synergistic interactions.

Applicant argues that none of the references cited provide the necessary motivation to predict the successful therapeutic benefits of combining imatinib with HDAC inhibitors. However, it is not necessary to provide motivation to predict the successful therapeutic benefits. Again, MPEP § 2143.02 states that obviousness requires only a reasonable expectation of success. The Examiner provided a prima facie obviousness rejection based on *In re Kerkhoven* and a motivation to combine based on Grant.

Applicant argues that the holding in *KSR International Co. v. Teleflex Inc.*, should not apply because the present invention relates to a different field of science and anticipated success in the pharmaceutical arts is difficult to ascertain. The ease or difficulty with which combinations are made was not determinative of the holding in KSR. KSR allows for analysis of obviousness that takes into account more than a teaching suggestion or motivation. This analysis can be applied to all areas of patentability. Moreover, applicant has not supplied a basis for restricting the holding of KSR to only the mechanical arts.

Applicant argues that combining two therapeutic agents for the treatment of a specific disease requires experimentation. However, MPEP § 2164.02 states that "[t]he

specification need not contain an example if the invention is otherwise disclosed in such manner that one skilled in the art will be able to practice it without an undue amount of experimentation. *In re Borkowski*, 422 F.2d 904, 908, 164 USPQ 642, 645 (CCPA 1970)." Again, the artisan need only have a reasonable expectation of success. Combination therapy in cancer treatment is well known and even encouraged, as evidenced by Grant. The artisan would have a reasonable expectation of success in combining imatinib and SAHA since both compounds are known for successfully treating leukemia.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). The combined teachings of the references provide motivation for the combination as well as the case law cited in *In re Kerkhoven*.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Walter E. Webb whose telephone number is (571) 270-3287. The examiner can normally be reached on 8:00am-4:00pm Mon-Fri EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick F. Krass can be reached (571) 272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Walter E. Webb
/Walter E Webb/
Examiner, Art Unit 1612

/Frederick Krass/

Supervisory Patent Examiner, Art Unit 1612